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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/046,517	01/14/2002	Imre Kovesdi	212518	3747
23460	7590	02/25/2004	EXAMINER	
LEYDIG VOIT & MAYER, LTD TWO PRUDENTIAL PLAZA, SUITE 4900 180 NORTH STETSON AVENUE CHICAGO, IL 60601-6780			DAVIS, RUTH A	
			ART UNIT	PAPER NUMBER
			1651	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/046,517	<b>Applicant(s)</b> KOVESDI ET AL.	
	<b>Examiner</b> Ruth A. Davis	<b>Art Unit</b> 1651	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 04 December 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-14 and 27-38 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-14 and 27-38 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Applicant's request for continued examination filed December 4, 2003 has been received and entered into the case. The submission filed November 3, 2003, has been entered and considered. Claims 15 – 26 are canceled; claims 27 – 38 are added; claims 1 – 14 and 27 – 38 are pending and have been considered on the merits. All arguments have been fully considered.

#### ***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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3. Claims 1 – 3, 6 – 10, 27 and 30 – 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Herrmann (US 5792643).

Applicant claims a composition for maintaining a non-enveloped viral vector, the composition comprising about 1 – 25% trehalose; about 0.05 – 1.5 mM divalent metal salt; a multiplicity of non-enveloped viral vector particles; and a liquid carrier. Specifically the composition comprises about 0.05 – 1 mM divalent metal salt, or 0.05 – 1 mM  $\text{MgCl}_2$ . The composition further comprises a buffer, such that the pH is about 6 – 9 at 25C and 10 – 65 mM arginine. The concentration of non-enveloped viral vectors are about  $1 \times 10^5$  –  $1 \times 10^{13}$  FFU/ml, the osmolality of the liquid composition is about 150 – 800 mOsM, the ionic strength of the liquid composition is about 10 – 200 mM.

Herrmann teaches stabilizing viral particles by adding thereto a saccharide, buffer and water (abstract). Specifically, compositions of buffer, 1 – 12% trehalose, 0.03% or less NaCl and 0.1 – 10% arginine are combined with a retrovirus to obtain an aqueous solution with a pH of about 7.4 (col.3, example 3). Other salts may also be added such as magnesium chloride (col.7 line 1-5).

Herrmann does not specifically teach the claimed amounts of each ingredient, the claimed osmolality or ionic strength. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize the amounts of known effective ingredients as well as osmolalities and ionic strengths, as a matter of routine experimentation. Therefore, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the parameters of the composition of

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Herrmann with a reasonable expectation for successfully obtaining a composition for stabilizing viruses.

4. Claims 1 – 9, 11 – 14, 27 – 33 and 35 – 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans (US 2002/0041881 A1) or Evans (WO 01/66137).

Applicant claims a composition for maintaining a non-enveloped viral vector, the composition comprising about 1 – 25% trehalose; about 0.05 – 1.5 mM divalent metal salt; a multiplicity of non-enveloped viral vector particles; and a liquid carrier. Specifically, the composition comprises about 0.05 – 1 mM divalent metal salt, or 0.05 – 1 mM  $\text{MgCl}_2$ . The composition further comprises a nonionic surfactant in about 0.001 – 0.015%, wherein the nonionic surfactant is polysorbate 80; and a buffer, such that the pH is about 6 – 9 at 25C. The concentration of non-enveloped viral vectors are about  $1 \times 10^5$  –  $1 \times 10^{13}$  PFU/ml, the osmolality of the liquid composition is about 150 – 800 mOsM and the ionic strength of the liquid composition is about 10 – 200 mM. The viral vector is an adenoviral vector and is replication deficient.

Evans (US) teaches viral compositions comprising a liquid adenovirus, buffer, sugar, salt, divalent cation and non-ionic detergent (abstract). The compositions are disclosed to maintain viral stability for up to 2 years at temperatures of 2 – 8C and higher (0004, 0012). Specifically, the composition comprises an adenovirus in an amount of  $1 \times 10^7$  virus particles/milliliter –  $1 \times 10^{13}$  particles/milliliter (0050). Non-ionic surfactants include polysorbate 80 (0051) at about 0.001 – 1% (0059), divalent cations include  $\text{MgCl}_2$  at about 0.1 – 5 mM (0052), and the 2 – 8% sugar/cryoprotectant may be trehalose (0053, 0060, 0061). Evans (US) teaches the salts are

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added to attain the desired ionic strength and osmolarity (0054) with preferred osmolarties between 200 – 800 mOs/L (0056) and a preferred pH of 7.5 – 8.5 (0059).

Evans (WO) teaches viral compositions comprising a liquid adenovirus, buffer, sugar, salt, divalent cation and non-ionic detergent (abstract). The compositions are disclosed to maintain viral stability for up to 2 years at temperatures of 2 – 8C and higher (p.1,3). Specifically, the composition comprises an adenovirus in an amount of  $1 \times 10^7$  virus particles/milliliter –  $1 \times 10^{13}$  particles/milliliter (p.8). Non-ionic surfactants include polysorbate 80 (p.9) at about 0.001 – 1% (p.11), divalent cations include  $MgCl_2$  at about 0.1 – 5 mM (p.9), and the sugar may be trehalose (p.9). Evans (WO) teaches the salts are added to attain the desired ionic strength and osmolarity (0054) with preferred osmolarties between 200 – 800 mOs/L (p.10) and a preferred pH of 7 – 9 (p.8).

The references do not teach the compositions with the claimed ionic strength, or wherein the virus is replication deficient. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize the parameters of the compositions of Evans (US) and/or Evans (WO) as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the parameters of the above compositions with a reasonable expectation for successfully obtaining a composition for maintaining a viral vector.

5. Claims 1 – 14 and 27 – 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kovesdi (WO 00/34444).

Applicant claims a composition for maintaining a non-enveloped viral vector, the composition comprising about 1 – 25% trehalose; about 0.05 – 1.5 mM divalent metal salt; a multiplicity of non-enveloped viral vector particles; and a liquid carrier. Specifically, the composition comprises about 0.05 – 1 mM divalent metal salt; or 0.05 – 1 mM  $\text{MgCl}_2$ . The composition further comprises a nonionic surfactant in about 0.001 – 0.015%, wherein the nonionic surfactant is polysorbate 80; a buffer, such that the pH is about 6 – 9 at 25C; and about 10 – 65 mM arginine. The concentration of non-enveloped viral vectors are about  $1 \times 10^5$  –  $1 \times 10^{13}$  PFU/ml, the osmolality of the liquid composition is about 150 – 800 mOsm and ionic strength of the liquid composition is about 10 – 200 mM. Finally, the viral vector is a replication deficient adenoviral vector.

Kovesdi teaches a composition for preserving a virus, the composition comprising a liquid carrier, viral particles, polysorbate 80, L-arginine and trehalose (abstract). The composition additionally comprises adenovirus (p.2 line 31-34, p.3 line 11-19), tris buffer, and salts (p.3 line 26-30). The trehalose is present at about 2 – 10%, the polysorbate is present at about 0.001 – 0.01% (p.4 line 4-12) while the temperature is from 2 – 37C (p.5 line 27-34), and the pH is from 6 – 9 (p.6 line 32-37). Kovesdi teaches the compositions comprising divalent metal salts to include  $\text{MgCl}_2$  (examples).

Kovesdi does not teach the composition with the claimed amounts of each ingredient, ionic strength, osmolality, or wherein the virus is replication deficient. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize the amounts of known effective ingredients as well as the parameters of the compositions of Kovesdi as a matter of routine experimentation. Moreover, at the time of the

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claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the parameters of the disclosed composition with a reasonable expectation for successfully obtaining a composition for preserving a virus.

6. Claims 1 – 14 and 27 – 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans (US) or Evans (WO) in view of Kovesdi (WO).

Applicant claims a composition for maintaining a non-enveloped viral vector, the composition comprising about 1 – 25% trehalose; about 0.05 – 1.5 mM divalent metal salt; a multiplicity of non-enveloped viral vector particles; and a liquid carrier. Specifically, the composition comprises about 0.05 – 1 mM divalent metal salt; or 0.05 – 1 mM  $\text{MgCl}_2$ . The composition further comprises a nonionic surfactant in about 0.001 – 0.015%, wherein the nonionic surfactant is polysorbate 80; a buffer, such that the pH is about 6 – 9 at 25C; and about 10 – 65 mM arginine. The concentration of non-enveloped viral vectors are about  $1 \times 10^5$  –  $1 \times 10^{13}$  PFU/ml, the osmolality of the liquid composition is about 150 – 800 mOsm and ionic strength of the liquid composition is about 10 – 200 mM. Finally, the viral vector is a replication deficient adenoviral vector.

Evans (US) teaches viral compositions comprising a liquid adenovirus, buffer, sugar, salt, divalent cation and non-ionic detergent (abstract). The compositions are disclosed to maintain viral stability for up to 2 years at temperatures of 2 – 8C and higher (0004, 0012). Specifically, the composition comprises an adenovirus in an amount of  $1 \times 10^7$  virus particles/milliliter –  $1 \times 10^{13}$  particles/milliliter (0050). Non-ionic surfactants include polysorbate 80 (0051) at about 0.001 – 1% (0059), divalent cations include  $\text{MgCl}_2$  at about 0.1 –

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5 mM (0052), and the 2 – 8% sugar/cryoprotectant may be trehalose (0053, 0060, 0061). Evans (US) teaches the salts are added to attain the desired ionic strength and osmolarity (0054) with preferred osmolarties between 200 – 800 mOs/L (0056) and a preferred pH of 7.5 – 8.5 (0059).

Evans (WO) teaches viral compositions comprising a liquid adenovirus, buffer, sugar, salt, divalent cation and non-ionic detergent (abstract). The compositions are disclosed to maintain viral stability for up to 2 years at temperatures of 2 – 8C and higher (p.1,3).

Specifically, the composition comprises an adenovirus in an amount of  $1 \times 10^7$  virus particles/milliliter –  $1 \times 10^{13}$  particles/milliliter (p.8). Non-ionic surfactants include polysorbate 80 (p.9) at about 0.001 – 1% (p.11), divalent cations include  $MgCl_2$  at about 0.1 – 5 mM (p.9), and the sugar may be trehalose (p.9). Evans (WO) teaches the salts are added to attain the desired ionic strength and osmolarity (0054) with preferred osmolarties between 200 – 800 mOs/L (p.10) and a preferred pH of 7 – 9 (p.8).

The references do not teach the compositions further comprising arginine. However, Kovesdi teaches a composition for preserving a virus, the composition comprising a liquid carrier, adenoviral particles, polysorbate 80, L-arginine, divalent salts and trehalose (abstract, p.2 line 31-34, p.3 line 11-19). At the time of the claimed invention, one of ordinary skill in the art would have been motivated to include arginine in the compositions of Evans (US) or Evans (WO) because of the known and disclosed use to preserve viruses. Moreover, at the time of the claimed invention, one or ordinary skill in the art would have been motivated to combine arginine to the composition of Evans (US) and/or Evans (WO) with a reasonable expectation for successfully obtaining a composition for preserving and maintaining viral compositions.

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The references do not teach the compositions with the claimed ionic strength, or wherein the virus is replication deficient. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize the parameters of the compositions of Evans (US) and/or Evans (WO) as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the parameters of the above compositions with a reasonable expectation for successfully obtaining a composition for maintaining a viral vector.

7. Claims 1 – 14 and 27 – 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kovesdi (WO) in view of Frei (WO 99/41416).

Applicant claims a composition for maintaining a non-enveloped viral vector, the composition comprising about 1 – 25% trehalose; about 0.05 – 1.5 mM divalent metal salt; a multiplicity of non-enveloped viral vector particles; and a liquid carrier. Specifically, the composition comprises about 0.05 – 1 mM divalent metal salt; or 0.05 – 1 mM  $MgCl_2$ . The composition further comprises a nonionic surfactant in about 0.001 – 0.015%, wherein the nonionic surfactant is polysorbate 80; a buffer, such that the pH is about 6 – 9 at 25°C; and about 10 – 65 mM arginine. The concentration of non-enveloped viral vectors are about  $1 \times 10^5$  –  $1 \times 10^{13}$  PFU/ml, the osmolality of the liquid composition is about 150 – 800 mOsm and ionic strength of the liquid composition is about 10 – 200 mM. Finally, the viral vector is a replication deficient adenoviral vector.

Kovesdi teaches a composition for preserving a virus, the composition comprising a liquid carrier, viral particles, polysorbate 80, L-arginine and trehalose (abstract). The

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composition additionally comprises adenovirus (p.2 line 31-34, p.3 line 11-19), tris buffer, and salts (p.3 line 26-30). The trehalose is present at about 2 – 10%, the polysorbate is present at about 0.001 – 0.01% (p.4 line 4-12) while the temperature is from 2 – 37C (p.5 line 27-34), and the pH is from 6 – 9 (p.6 line 32-37). Kovesdi teaches the compositions comprising divalent metal salts to include MgCl<sub>2</sub> (examples).

Kovesdi does not teach the composition with the claimed amounts of each ingredient, ionic strength, osmolality, or wherein the virus is replication deficient. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize the amounts of known effective ingredients as well as the parameters of the compositions of Kovesdi as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the parameters of the disclosed composition with a reasonable expectation for successfully obtaining a composition for preserving a virus.

Kovesdi does not teach a specific composition of trehalose and MgCl<sub>2</sub>. However, Frei teaches compositions comprising adenoviral particles buffered to maintain a pH of 7 – 8.5 in the temperatures of 2 – 27C (abstract, p.8) wherein the compositions comprise about 5 – 25 mg/mL disaccharides, about  $1 \times 10^9$  –  $1 \times 10^{13}$  viral particles/mL (p.7), about 0.1 – 1 mg/mL divalent metal salts (magnesium salts) (p.5), diluents and about 0.01 – 0.3 mg/mL polysorbate 80 (p.7).

At the time of the claimed invention, one of ordinary skill in the art would have been motivated to use magnesium chloride as the salt of Kovesdi because of the known and disclosed use to preserve viruses. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to include MgCl<sub>2</sub> in the composition Kovesdi with a

reasonable expectation for successfully obtaining a composition for preserving and maintaining viral compositions.

### ***Double Patenting***

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1 – 14 and 27 – 38 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12 – 24 of U.S. Patent No. 6514943 or claims 13 – 20 of U.S. Patent No. 6225289 in view of Evans (US) and/or Evans (WO).

US Patent 6514943 claims a composition comprising an adenovirus, liquid carrier, and stabilizing agents selected from polysorbate 80, L-arginine, trehalose, or combinations thereof. The composition has 2 – 10% trehalose.

US 6225289 claims a liquid composition comprising adenoviral vector, liquid carrier, and a stabilizing agent selected from polysorbate 80, L-arginine, trehalose and combinations thereof. Specifically, 2 – 10% trehalose, 0.001 – 0.1% polysorbate 80, a buffer and salt.

Although the claims do not teach the composition comprising MgCl<sub>2</sub>, Evans (US) and Evans (W) teach viral compositions comprising a liquid adenovirus, buffer, sugar, salt, divalent cation and non-ionic detergent. The compositions are disclosed to maintain viral stability for up to 2 years at temperatures of 2 – 8°C and higher. Specifically, the composition comprises an adenovirus in an amount of  $1 \times 10^7$  virus particles/milliliter –  $1 \times 10^{13}$  particles/milliliter. Non-ionic surfactants include polysorbate 80 at about 0.001 – 1%, divalent cations include MgCl<sub>2</sub> at about 0.1 – 5 mM, and the 2 – 8% sugar/cryoprotectant may be trehalose. Evans teaches the salts are added to attain the desired ionic strength and osmolarity with preferred osmolarties between 200 – 800 mOs/L and a preferred pH of 7.5 – 8.5. Evans teaches that the MgCl<sub>2</sub> is necessary for optimum adenovirus stability (example 5).

At the time of the claimed invention, one of ordinary skill in the art would have been motivated to use magnesium chloride as the salt of Kovesdi because of the known and disclosed use to stabilize, maintain and preserve viruses. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to include MgCl<sub>2</sub> in the composition Kovesdi with a reasonable expectation for successfully obtaining a composition for preserving and maintaining viral compositions.

In addition, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize the amounts of known effective ingredients

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as well as the parameters (ionic strength, osmolalities) of the compositions of Kovesdi as a matter of routine experimentation.

### ***Response to Arguments***

Applicant argues that while the references do teach salts such as MgCl<sub>2</sub> in their compositions, they do not teach the claimed amounts of 0.05 – 1.5 mM. Applicant additionally submits a declaration, stating that example 3 demonstrates smaller amounts of MgCl<sub>2</sub> have an unexpectedly better stabilizing effect than greater amounts.

However, these arguments fail to persuade because as stated above, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to optimize volumes of active ingredients as a matter of routine experimentation. In support, Herrmann teaches the salts at less than 0.03%, Evans (US and WO) teaches MgCl<sub>2</sub> at 0.1 – 5mM and Frei teaches 1 – 10 mM MgCl<sub>2</sub>. In further support, Nyberg-Hoffman et al. (1999) teaches solutions for preserving/stabilizing solutions for adenoviral storage comprising 2 mM MgCl<sub>2</sub> (p.955, 957). It is noted that each of the references teach a range which includes the claimed amount of MgCl<sub>2</sub>. As evidenced by the cited references, optimizing the amount of MgCl<sub>2</sub> was routinely practiced in the art at the time of the claimed invention. Moreover, at the time of the claimed invention, one of ordinary skill in the art would certainly have been motivated to optimize the amount of MgCl<sub>2</sub> with a reasonable expectation for successfully obtaining an effective composition for maintaining non-enveloped viral vectors.

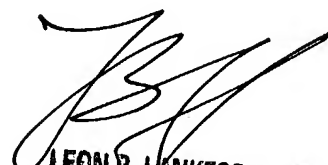
Regarding the declaration, the evidence is not commensurate in scope with the claims. Specifically, the claims include 1 – 25% trehalose whereas example 3 demonstrates the composition comprising sucrose. As such, the example fails to provide factual evidence of an unexpected result relative to the claimed composition. Furthermore, as stated above, the claimed amount falls within the disclosed ranges of  $MgCl_2$  in the references cited.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 571-272-0915. The examiner can normally be reached on M-H (7:00-4:30); alt. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ruth A. Davis; rad  
February 19, 2004.

  
LEON R. LANKFORD, JR.  
PRIMARY EXAMINER